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JAMDA 24 (2023) 419–425

JAMDA

journal homepage: www.jamda.com

Original Study

Cognitive Decline Before and During COVID-19 Pandemic Among Older People With Multimorbidity: A Longitudinal Study

Chenglong Li BSc [a,b], Rong Hua MSc [a,b], Darui Gao MSc [a,b], Fanfan Zheng PhD [c,*], Wuxiang Xie PhD [a,b,*]

[a] Peking University Clinical Research Institute, Peking University First Hospital, Beijing, China
[b] PUCRI Heart and Vascular Health Research Center at Peking University Shougang Hospital, Beijing, China
[c] School of Nursing, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China

Keywords:
COVID-19
multimorbidity
cognitive decline
dementia

A B S T R A C T

Objective: To investigate whether older people living with multimorbidity would suffer an accelerated decline in cognition during the COVID-19 pandemic, compared with prepandemic data.
Design: A 5-year cohort conducting surveys from year 2016 to 2021, with 2016 to 2019 as the control period and 2019 to 2021 the pandemic period.
Setting and Participants: In total, 9304 cognitively healthy older participants age ≥50 years were included from the Health and Retirement Study (HRS).
Methods: Multimorbidity was defined as the concurrent presence of 2 or more chronic diseases. A global cognition *z* score was calculated using memory (immediate and delayed word recall tests) and executive function (counting backwards and the serial sevens tests). Incident dementia was defined using either the reported physician diagnosis or an alternative approach based on cognition summary score. Linear mixed models were used to assess longitudinal changes, while modified Poisson regression models were used to analyze the risk of incident dementia.
Results: Of the 9304 participants included, 3649 (39.2%) were men, with a mean age of 65.8 ± 10.8 years. Participants with multimorbidity (n = 4375) suffered accelerated declines of 0.08 standard deviation (95% confidence interval 0.03, 0.13, $P = .003$) in global cognition and an elevated dementia risk (risk ratio 1.66, 95% confidence 1.05 to 2.61, $P = .029$), compared with individuals without morbidity (n = 1818) during the pandemic period. After further adjusting sociodemographic characteristics and prepandemic cognitive measurements, these differences remained evident. In contrast, no significant differences in cognitive declines were observed during the control period.
Conclusions and Implications: During the COVID-19 pandemic, older people with multimorbidity suffered an accelerated decline in cognition and elevated incident dementia risk, while no evident differences in cognitive decline rates were observed before the pandemic. Measures targeting vulnerable older people with multimorbidity could be significant for assisting these individuals to tackle neurocognitive challenges during the pandemic.

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The present study was supported by the National Natural Science Foundation of China (project no. 81974490), the Non-profit Central Research Institute Fund of Chinese Academy of Medical Sciences (2021-RC330-001) and 2019 Irma and Paul Milstein Program for Senior Health Research Project. The funder had no role in the study design; the collection, analysis, and interpretation of data; the writing of the manuscript; or the decision to submit the article for publication.

The authors declare no conflicts of interest.

Author contributions: Chenglong Li contributed to the formal analysis and writing the original draft. Rong Hua and Darui Gao contributed to data curation and manuscript editing efforts. Fanfan Zheng and Wuxiang Xie conceptualized the study design and funding acquisition, as well as manuscript reviewing and editing efforts. All authors had full access to the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. Fanfan Zheng and Wuxiang Xie are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Data availability statement: Original survey dataset from the HRS is freely available to all bonafide researchers. Access to data can be obtained by visiting their websites (https://hrs.isr.umich.edu/about).

* Address correspondence to Fanfan Zheng, PhD, School of Nursing, Peking Union Medical College, 33 Ba Da Chu Road, Shijingshan District, 100144 Beijing, China; or Wuxiang Xie PhD, Peking University Clinical Research Institute, Peking University First Hospital, No. 8 Xishiku Street, Xicheng District, 100034 Beijing, China.

E-mail addresses: zhengfanfan@nursing.pumc.edu.cn (F. Zheng), xiewuxiang@hsc.pku.edu.cn (W. Xie).

https://doi.org/10.1016/j.jamda.2023.01.001
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The Coronavirus disease 2019 (COVID-19) pandemic has brought substantial changes to people's lives across the world, posing unprecedented challenges to health care systems. Older people are particularly vulnerable to devastating consequences of the pandemic, compared with the younger generations, not only because of elevated risks of hospitalization and death from COVID-19 disease, but also the diminished social contact, ever-increasing constraints on movement, and the loss of health care provided for non-COVID-19 illnesses.[1] Evaluating the potential impact of the pandemic on mental health across the whole population is regarded as one major priority, with vulnerable groups of older ages in particular.[2]

Multimorbidity is one important characteristic of older people (eg, the presence of 2 or more chronic diseases irrespective of the severity of such conditions.[3] Even before the pandemic, studies found that older people living with multimorbidity would face an increased dementia risk.[4] During the pandemic, challenges arising from social isolation and diminished access to care could further exacerbate the cognitive deterioration among these vulnerable individuals. So far, there still lacks longitudinal data on how the COVID-19 pandemic would impact the cognition of these individuals, compared with prepandemic cognitive measurements.

Hence, our purpose is to evaluate the cognitive decline before and during the COVID-19 pandemic of older people living with multimorbidity, as well as the incident dementia risk during the pandemic. Data came from the Health and Retirement Study (HRS), a national-representative prospective cohort conducting regular biennial surveys in the United States. We hypothesized that during the COVID-19 pandemic, older people living with multimorbidity, compared with no morbidity individuals, would suffer an accelerated cognitive decline and elevated incident dementia risk.

Methods

Study Design

The HRS is a prospective and nationally representative cohort of community-dwelling adults age ≥50 years in the United States. Details regarding its objectives, design, and survey content can be accessed elsewhere.[5] The HRS started in 1992 and repeated regular surveys, namely wave, in a biennial fashion. Before wave 14 (2018 to 2019), the HRS team conducted both face-to-face and telephone interviews in the household. Since wave 14, the web interview was administered as an alternate mode to face-to-face and telephone interviews. To be eligible for the web interview, participants have to (1) with internet connection; (2) English speaking; (3) self-respondent; (4) not identified as a nursing-home resident in the prior wave. We used survey data from waves 13 to 14 (2016 to 2019) as the control period, and waves 14 to 15 (2019 to 2021) as the pandemic period. Wave 14 was considered as the baseline. The study timeline and design were presented in Figure 1. Participants were excluded if they (1) missing cognitive measurements at any waves from 13 to 15; (2) with recorded dementia at waves 13 or 14. The HRS was approved by the Institutional Reviewing Board at the University of Michigan and the National Institute on Aging (HUM00061128). All participants provided written informed consent prior to inclusion for each survey. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline, with reporting checklist provided as part of the Supplementary Materials.

Multimorbidity Evaluation

Six chronic diseases were considered, including hypertension, diabetes, stroke, heart diseases, chronic lung diseases, and cancer. Hypertension was defined as a physician-confirmed formal diagnosis or mean systolic blood pressure/diastolic blood pressure ≥140/90 mm Hg or the regular use of antihypertensive medications. Diabetes was defined as a physician-confirmed formal diagnosis or fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L), or the regular insulin injection. The remaining 4 diseases were all defined as the physician-confirmed formal diagnosis, including (1) stroke or transient ischemic attack; (2) heart attack, coronary heart disease, angina, congestive heart failure, or other heart diseases; (3) chronic lung diseases such as chronic bronchitis or emphysema except asthma; (4) cancer or a malignant tumor of any kind except skin cancer. Multimorbidity was defined as the concurrent presence of 2 or more diseases.[4]

Cognitive Function and Dementia Evaluation

The HRS administered several cognitive batteries. We used tests for memory and executive function, which could cover participants of all age groups. For memory, tests of immediate and delayed word recall of 10 unrelated words were used, with 1 point assigned for each word recalled, resulting in a score ranging from 0 to 20. For executive function, tests including the counting backwards (0–2 points) and the serial sevens (0–5 points) were implemented. For the counting backwards test, participants were asked to do backwards counting from 20 as quickly as they could, with 2 points assigned for either consecutive count from 19 to 10 or 20 to 11 on the first try and 1 point

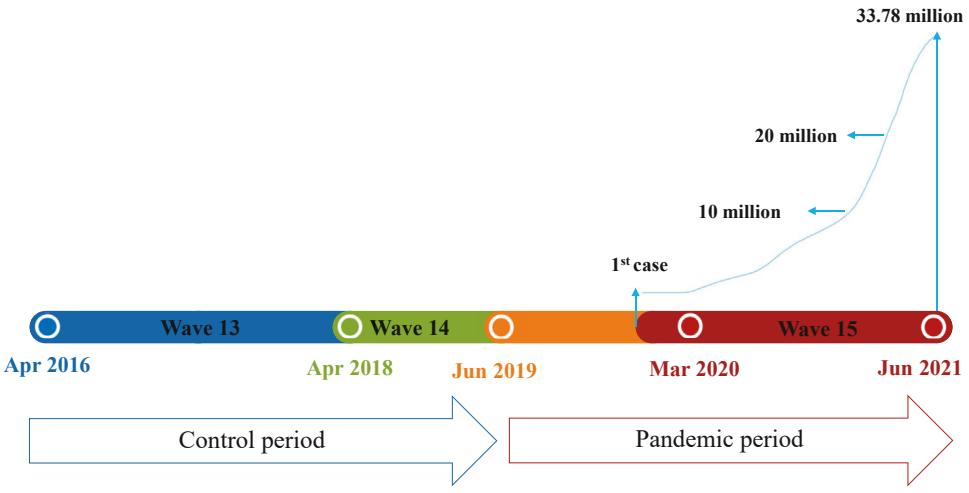

Fig. 1. Study timeline and design.

assigned for the successful count on the second try. For the serial sevens test, participants were asked to count by subtracting seven from 100 and continue subtracting until 5 subtractions were completed, with 1 point allocated for each correct subtraction. For all tests, a higher score indicated better cognitive performance, with validity and consistency verified by previous studies.[6-8] A global and subdomain cognition *z* scores were calculated, using baseline mean and standard deviation (SD) of raw cognition scores. Therefore, a cognition *z* score of −1 at any given wave indicated that the score was 1 SD below the mean cognitive score at baseline. Such approach for handling cognition raw scores has been widely embraced by previous studies.[6,8]

Evaluation of dementia cases comprised of a self-reported physician diagnosis of dementia and an alternative approach using the cognition summary score, which was the sum of raw memory and executive function scores. Using the cognition summary score ranging from 0 to 27, a participant would be defined as having dementia if he/she (1) reported a physician confirmed formal diagnosis of dementia or Alzheimer's disease; or (2) had a cognition summary score of 6 or less. Such an alternate approach for defining dementia was developed and verified using the same HRS samples by previous studies.[9,10]

Covariates

All study covariates were assessed at the baseline. Covariates adjusted included age (years), sex, ethnicity (of white ethnicity or not), cohabitation status (living alone or not), education background (less than high school, high school or equivalent, college and above), current smoking (yes or no), alcohol consumption (at least 3 days per week), physical activity participation (engaging in vigorous or moderate activities no less than once weekly), and depressive symptoms (≥4 points using an 8-item version of the Center for Epidemiologic Studies Depression Scale). For analysis regarding incident dementia, the baseline cognition summary score was also adjusted.[11]

Statistical Analysis

The mean ± SD was used for descriptive statistics of continuous variables and numbers (percentage) for categorical variables. Differences between groups were tested using the analysis of variance (*t* test for 2 groups), or the χ^2 test.

We used linear mixed-effects models to analyze cognitive decline. The intercept and the categorical time variable (indicating waves 13 to 15) were fitted as random effects at the individual level to account for between-participant differences at baseline and longitudinal changes. The Toeplitz covariance structure was selected to model within-participant correlations between repeated measurements, with Kenward–Roger adjustment to address the upward bias of test statistics for fixed model effects.[12]

We built 2 sets of linear mixed-effects models to analyze cognitive decline before and during the COVID-19 pandemic, respectively. The first set of models was confined to cognitive measurements during the control period, while the second to measurements during the pandemic period, respectively. The least-square means were computed to estimate the adjusted differences between changes.

The modified Poisson regression models were used to analyze the risk of incident dementia during the pandemic period, with the robust sandwich estimator applied for the calculation of risk ratio (RR) and the 95% confidence interval (CI).[13]

Several sensitivity analyses were conducted. First, to examine whether associations of multimorbidity with neurocognitive outcomes could be driven by individual chronic diseases, we adjusted for each of the 6 diseases, respectively. Second, to evaluate potential interactions with demographics and some measurements during the pandemic, an exploratory subgroup analysis was conducted. Variables defining subgroups included age (<65 and ≥65 years), sex, whether encountering COVID-19 infection or death of known people (family members or friends), and whether suffering delayed care (medical or dental care) during the pandemic. Third, a nonresponse analysis was conducted to evaluate the potential selection bias by comparing baseline characteristics between included and excluded participants. Fourth, to further address the potential selection bias from excluded participants, an inverse probability weighting approach (IPW) was applied. Such approach was used to reweight the included study sample, and the analytical weight for each individual was calculated as the inverse of the probability of being included in the analysis.[14] We used binary logistic regression to estimate the individual probability of being included in analysis, which included identical covariates with the primary analysis and the six individual chronic diseases. Love plot was used to visualize the absolute standardized mean differences between included and excluded participants.[15] Fifth, we further controlled for blood pressure status (mean systolic blood pressure/diastolic blood pressure ≥140/90 mm Hg or not, with missing values assigned as a single category), blood glucose status (fasting plasma glucose ≥126 mg/dL or not, with missing values assigned as a single category), the regular use of insulin and antihypertensive medications in our models, to further account for the associations between these variables and cognitive outcomes during the pandemic. Finally, considering the broad presence of the comorbidity of diabetes and hypertension, we modified our categorization by splitting it into no morbidity, 1 morbidity without hypertension or diabetes, 1 morbidity with hypertension or diabetes, ≥2 morbidities without the co-presence of hypertension and diabetes, and ≥2 morbidities with the co-presence of hypertension and diabetes. Then, we further examined the association between the modified multimorbidity categorization and incident dementia risk during the pandemic.

Statistical analysis was conducted using SAS v 9.4 (SAS Institute), with a 2tailed alpha of 0.05 considered statistically significant.

Results

Of the 9304 participants included, 3649 (39.2%) were men and 5825 (62.6%) were white, with a mean age of 65.8 ± 10.8 years, the detailed inclusion process of which was presented in Supplementary Figure 1. Compared with participants of no morbidity (n = 1818), those living with 1 morbidity (n = 3111) and of ≥2 morbidities (n = 4375) were significantly older, less educated, more likely to be alone, and less physically active, with a higher prevalence of depressive symptoms and worse cognition score, as shown in Table 1. The distribution of morbidities was presented in Supplementary Figure 2, with hypertension, diabetes, and heart diseases being the top 3 prevalent chronic conditions among people living with multimorbidity.

As presented in Table 2, during the control period, both participants living with 1 morbidity and multimorbidity did not differentiate in changes of global cognition, memory and executive function from their no morbidity counterparts. By contrast, during the pandemic period, participants living with multimorbidity suffered significantly accelerated declines of 0.08 SD (95% CI 0.03, 0.13, $P = .003$) in global cognition, 0.06 SD (95% CI 0.01, 0.12, $P = .042$) in memory, and 0.06 SD (95% CI 0.01, 0.11, $P = .023$) in executive function, compared with no morbidity individuals. However, those living with 1 morbidity continued to show no significant differences in cognitive changes from their no morbidity counterparts, as identical in global cognition, memory, and executive function. The estimated mean cognitive trajectories were depicted in Figure 2. As shown in Figure 2, before the pandemic (wave 13 to wave 14), similar changes in global cognition, memory, and executive function were identified among participants with different multimorbidity statuses, while comparatively sharp

Table 1
Baseline Characteristics of Participants by Multimorbidity Status

Characteristics*	All (n = 9304)	Multimorbidity Status			
		No Morbidity (n = 1818)	1 Morbidity (n = 3111)	≥2 Morbidities (n = 4375)	P†
Age (y)	65.8 ± 10.8	60.3 ± 9.1	64.7 ± 10.4	68.8 ± 10.7	<.001
Men (%)	3649 (39.2%)	654 (36.0%)	1192 (38.3%)	1803 (41.2%)	<.001
White (%)	5825 (62.6%)	1201 (66.1%)	1907 (61.3%)	2717 (62.1%)	.002
Living alone (%)	3521 (37.8%)	548 (30.1%)	1172 (37.7%)	1801 (41.2%)	<.001
Education background (%)					
Less than high school	1530 (16.4%)	225 (12.4%)	497 (16.0%)	808 (18.5%)	<.001
High school or equivalent	3070 (33.0%)	538 (29.6%)	978 (31.4%)	1554 (35.5%)	
College and above	4704 (50.6%)	1055 (58.0%)	1636 (52.6%)	2013 (46.0%)	
Current smoking (%)	1259 (13.5%)	267 (14.7%)	433 (13.9%)	559 (12.8%)	.100
Drinking ≥ 3 d per wk (%)	1479 (15.9%)	352 (19.4%)	533 (17.1%)	594 (13.6%)	<.001
Physical exercise (%)	6562 (70.5%)	1475 (81.1%)	2336 (75.1%)	2751 (62.9%)	<.001
Depressive symptoms (%)	1297 (13.9%)	185 (10.2%)	349 (11.2%)	763 (17.4%)	<.001
Total cognition score	15.9 ± 3.9	17.0 ± 4.0	16.2 ± 3.9	15.2 ± 3.8	<.001
Memory score	10.5 ± 3.1	11.3 ± 3.2	10.7 ± 3.1	9.9 ± 3.0	<.001
Executive function score	5.4 ± 1.7	5.7 ± 1.6	5.4 ± 1.7	5.3 ± 1.8	<.001

*Data are presented as mean ± SD or n (%).
†*P* value reported for differences between 3 groups using analysis of variance or χ^2 test.

declines in cognition were observed among multimorbidity individuals after the pandemic (wave 14 to wave 15).

During the pandemic period, a total of 277 incident dementia cases were identified. As presented in Table 3, an elevated risk for incident dementia was identified for multimorbidity participants, compared with no morbidity individuals. Such differences remained evident even after adjusting for baseline cognition score (RR 1.66, 95% CI 1.05 to 2.61, $P = .029$), as presented in model 3 of Table 3. Likewise, no significant difference in dementia risk was observed between participants with 1 morbidity and participants without morbidity.

As illustrated in results from Supplementary Table 1, when the 6 chronic diseases were adjusted individually, no material changes were observed, with significantly accelerated cognitive declines consistently identified for multimorbidity individuals. However, as shown in Supplementary Table 2, when hypertension and diabetes were adjusted individually, the RR for incident dementia became attenuated and statistically insignificant, with hypertension in particular.

No significant interactions with other subgroup variables were identified, as shown in results from Supplementary Tables 3–7. As shown in Supplementary Table 8, a total of 7842 participants were excluded from the analysis, who were comparatively older, with a higher prevalence of multimorbidity and worse cognitive performance.

After the IPW weighting, as shown in Supplementary Figure 3, differences between included and excluded participants were considerably diminished. According to analysis based the reweighted IPW samples, no material changes in primary results were observed, as shown in Supplementary Tables 9 and 10.

As shown in Supplementary Table 11, when the blood pressure, blood glucose, and corresponding treatments were adjusted in the models analyzing cognitive decline during the pandemic, identical results were observed, with significantly accelerated cognitive declines consistently identified for multimorbidity individuals for all cognitive domains. However, as shown in Supplementary Table 12, when the blood pressure, blood glucose, and corresponding treatments were simultaneously adjusted in the models, the RR for incident dementia became attenuated and statistically insignificant. After re-analyzing the association between multimorbidity status according to diabetes and hypertension and incident dementia risk, shown in Supplementary Table 13, only individuals of ≥2 morbidities with the co-presence of hypertension and diabetes were consistently associated with elevated dementia risk after other factors and the baseline cognition score were adjusted in the models.

Discussion

Based on the 5-year longitudinal data from the HRS, we found that during the COVID-19 pandemic, older people living with multimorbidity suffered an accelerated cognitive decline, compared with their no morbidity counterparts. By contrast, no evident differences in cognitive decline rates were observed during the control period before the pandemic. In addition, older people with multimorbidity suffered an elevated incident dementia risk during the pandemic. These differences remained evident even after controlling prepandemic measurements, including cognitive measurements and sociodemographic characteristics. These findings not only revealed the potential impact of the COVID-19 pandemic on the cognition of older people, but spotlighted individuals with multimorbidity who could be particularly vulnerable to an accelerated cognitive decline and elevated dementia risk during the pandemic. To our knowledge, this is the first prospective study to evaluate the potential impact of the COVID-19 pandemic on cognition via comparison with prepandemic longitudinal measurements, and simultaneously identify potentially vulnerable groups by examining associations between multimorbidity status with neurocognitive outcomes during the pandemic.

Previous studies also evaluated the potential impact of the pandemic on cognition. A cohort study involving 132 participants with dementia found that individuals evaluated during the pandemic suffered an accelerated cognitive decline, compared with the other participants evaluated before the pandemic.[16] The authors concluded that COVID-19 pandemic have induced a significant worsening of cognitive decline in people with dementia, highlighting the need for tackling the detrimental consequences of social isolation measures.[16] Although the study introduced the control group with cognitive measurements before the pandemic, it was the intergroup comparison being conducted (eg, participants being compared were not identical before and during the pandemic), thus, further limiting the ability to make direct inferences.[16] Another study evaluated the potential impact of COVID-19 lockdown on cognition among 1215 general adults and found there were significant deteriorations in both subjective cognitive functioning and mental health, compared with measurements before the lockdown.[17] A longitudinal study also assessed the neurocognitive impact of the pandemic.[18] They included 467 community-dwelling older adults age ≥65 years, and identified a significant acceleration in annual cognitive decline rate during the pandemic, in comparison with the prior 15-year measurements.[18] Despite the shared findings, these contributions either did not introduce the control period using

Table 2
Mean Differences in Changes of Global and Subdomain Cognition *z* Scores Between Multimorbidity Status Groups, by Study Periods

Multimorbidity Status	Global *z* Score		Memory *z* Score		Executive Function z Score	
	β (95% CI)*	*P*	β (95% CI)	*P*	β (95% CI)	*P*
Control period						
No morbidity	Reference	/	Reference	/	Reference	/
1 morbidity	−0.02 (−0.07, 0.04)	.562	−0.03 (−0.10, 0.03)	.273	0.01 (−0.04, 0.06)	.693
≥2 morbidities	−0.03 (−0.08, 0.02)	.193	−0.04 (−0.10, 0.02)	.199	−0.01 (−0.06, 0.03)	.588
Pandemic period						
No morbidity	Reference	/	Reference	/	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497	0.04 (−0.03, 0.10)	.263	−0.01 (−0.06, 0.04)	.776
≥2 morbidities	−0.08 (−0.13, −0.13)	.003	−0.06 (−0.12, −0.12)	.042	−0.06 (−0.11, −0.11)	.023

*Adjusted for age, sex, and education background, race, cohabitation status, current smoking, alcohol consumption, physical activity participation, and depressive symptoms.

longitudinal cognitive measurements before the pandemic or could not be able to make inferences based on large nationally representative samples. Hence, our study further consolidated findings regarding the potential neurocognitive impact of the COVID-19 pandemic by filling the current research gaps.

In addition, we identified the vulnerability of older people living with multimorbidity to cognitive decline and incident dementia risk during the pandemic. Further sensitivity analysis showed such vulnerability to cognitive decline could be independent of single chronic conditions, with consistent findings observed irrespective of which of the 6 individual conditions was adjusted. It should be noted that the vulnerability of older people living with multimorbidity to cognitive decline also could be independent of the comorbidity of hypertension and diabetes, with identical results observed before and after controlling for the combination of blood pressure, blood glucose, and regular use of antihypertensive medications and insulin. Interestingly, the observed associations between multimorbidity and incident dementia risk became insignificant when hypertension and

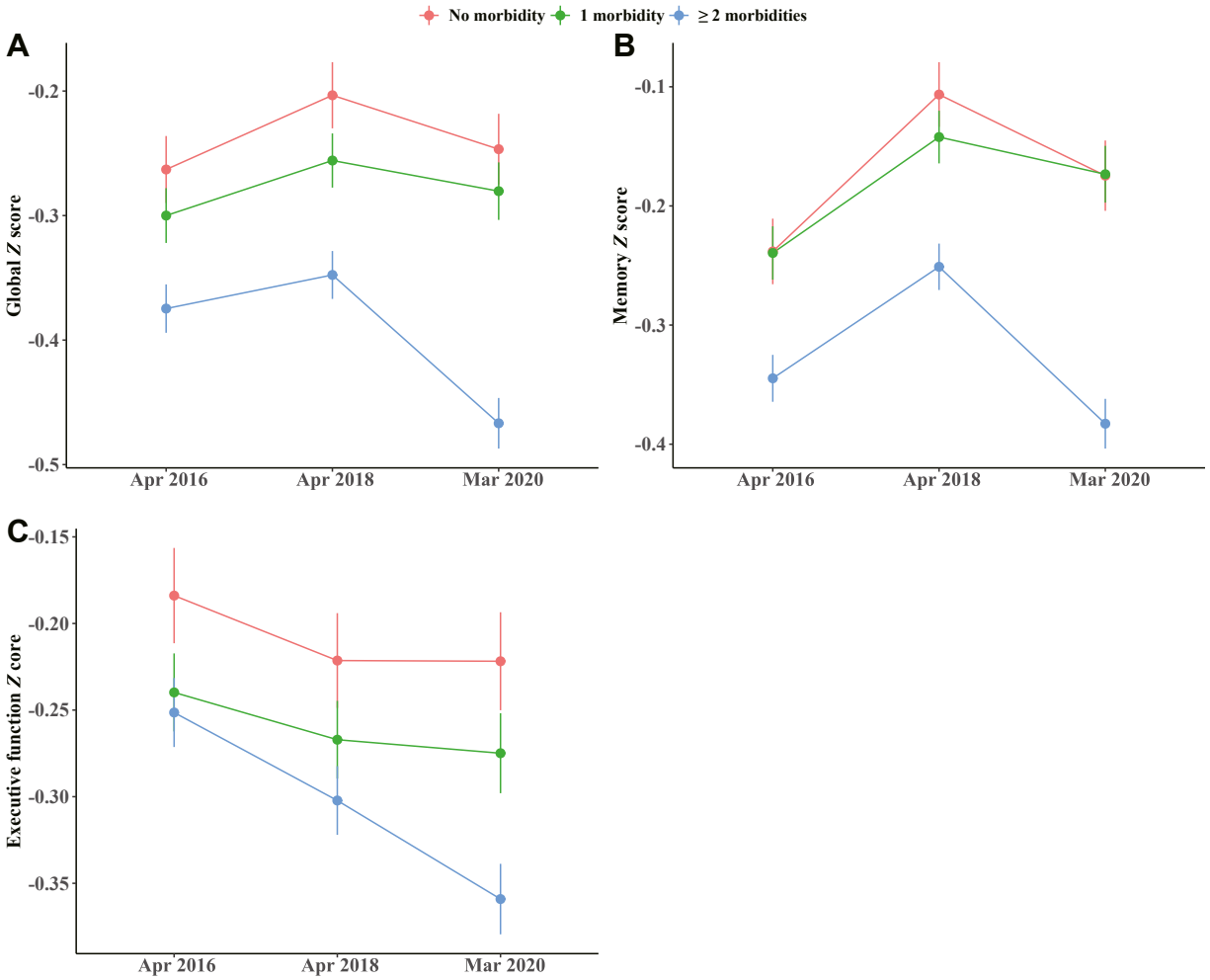

Fig. 2. Estimated mean cognitive trajectories by multimorbidity status. Points represent estimated mean cognition scores by linear mixed models from Table 2, while vertical lines represent standard errors. Adjusted covariates were identical to results in Table 2.

Table 3
Associations of Multimorbidity Status With Incident Dementia Risk During the Pandemic Period

Multimorbidity Status	Events/Total	Risk for Incident Dementia	
		RR (95% CI)	*P*
Model 1*			
No morbidity	21/1818	Reference	/
1 morbidity	70/3111	1.47 (0.91, 2.40)	.119
≥2 morbidities	186/4375	2.25 (1.41, 3.59)	<.001
Model 2†			
No morbidity	21/1818	Reference	/
1 morbidity	70/3111	1.33 (0.82, 2.17)	.245
≥2 morbidities	186/4375	1.89 (1.19, 3.01)	.007
Model 3‡			
No morbidity	21/1818	Reference	/
1 morbidity	70/3111	1.31 (0.82, 2.11)	.258
≥2 morbidities	186/4375	1.66 (1.05, 2.61)	.029

*Model 1: adjusted for age, sex, and education background.
†Model 2: model 1 + race, cohabitation status, current smoking, alcohol consumption, physical activity participation, and depressive symptoms.
‡Model 3: model 2 + baseline cognition summary score.

diabetes, or the combination of blood pressure, blood glucose, and regular use of antihypertensive medications and insulin, were included in the model. Further categorization analysis showed that only individuals living with the comorbidity of hypertension and diabetes were consistently associated with elevated dementia risk. Such findings indicated that the comorbidity of hypertension and diabetes could be the main contributors to elevated dementia risk among older people living with multimorbidity. According to previous studies, both hypertension and diabetes are 2 main attributable risk factors for dementia.[19] And future studies with large sample sizes would be warranted to further examine how the pattern of multimorbidity is associated with the dementia risk.

There are 2 major implications of our findings. First, the impact of the COVID-19 pandemic on the neurocognitive health of older people required attention. According to the 2022 Alzheimer's disease facts and figures, there were 15,925 more deaths from Alzheimer's disease and 44,729 more deaths from all dementias in 2020, compared with the average of the 5 years before 2020, corresponding to 13% and 17% more than expected numbers, respectively.[20] These facts indicated that the COVID-19 pandemic has had a dramatic effect on mortality from Alzheimer's disease and other dementias in the United States.[20] Moreover, the pandemic also posed unprecedented challenges to current dementia caregiving. Because of the strict lockdown procedures in the early stage of the pandemic, many caregivers were confronted with barriers to fulfilling the service, causing emotional distress and other negative outcomes.[20] Such challenges could translate to worsen care for dementia and, together with the pandemic's disruptions to other general and brain-related health care services for older people, explained the comparatively deteriorated cognition during the pandemic we observed. Second, older people living with multimorbidity could be in extra need of improved care and support to tackle the more severe neurocognitive challenges. As indicated by other studies, older people with multimorbidity also could suffer worse prognoses after infection and poor mental health outcomes during the pandemic.[21-23] Therefore, early identification and timely intervention of these vulnerable older individuals could be of great significance, especially in an era when the aging-related health challenges are further aggravated by the COVID-19 catastrophe.

Our study possesses several strengths. First, based on the longitudinal cognitive measurements before the pandemic, we were able to introduce the control period for comparison. Such design enabled us a stronger capability in inferring the potential neurocognitive impact of the pandemic. Second, our findings were robust, with generally consistent findings broadly observed in both the main and sensitivity analyses. Finally, our findings were based on a nationally representative sample of the older people age ≥50 years in the United States. Because of the implementation of both telephone and web interviews, older adults with restricted access to the internet could also participate in the survey. Our population also included a large proportion of individuals of other races than White, resulting in enhanced generalizability of study findings.

Several limitations also require attention. First, the cognitive batteries used in our study were less comprehensive for a formal cognitive evaluation. Although the HRS cohort also conducted other cognitive tests, only the memory and executive function tests could cover participants of all age ranges. Therefore, we were not able to capture the preclinical decline in cognitive domains other than the 2 implemented tests, leading to potential bias. Second, no formal clinical evaluation was conducted to further confirm the dementia diagnosis. Despite an alternative and verified approach being applied for defining dementia cases, only deficits in memory and executive function domains were included for evaluation. Hence, those impaired cognitions other than the 2 domains could have been missed, leading to potential underestimated dementia incidence. Finally, many participants were excluded, leading to potential selection bias. Despite an IPW sensitivity analysis was conducted, such bias still could not be neglected.

Conclusions and Implications

In summary, we found that during the COVID-19 pandemic, older people with multimorbidity aged ≥50 years in the United States suffered an accelerated decline in cognition compared with their no morbidity counterparts. By contrast, no evident differences in cognitive decline rates were observed during the control period. In addition, older people with multimorbidity were also vulnerable to incident dementia risk during the pandemic. It could be necessary for providing neuropsychological services to improve cognitive health during the pandemic. Meanwhile, public health measures should consider the need for the care of older vulnerable people already living with multimorbidity, and be developed for immediate provision of targeted interventions to assist these individuals to tackle neurocognitive challenges during the pandemic.

Acknowledgments

We appreciate efforts made by the original data creators, depositors, copyright holders, the funders of the data collections, and their contributions to the access of data from the Health and Retirement Study (waves 13 Supplemental 15).

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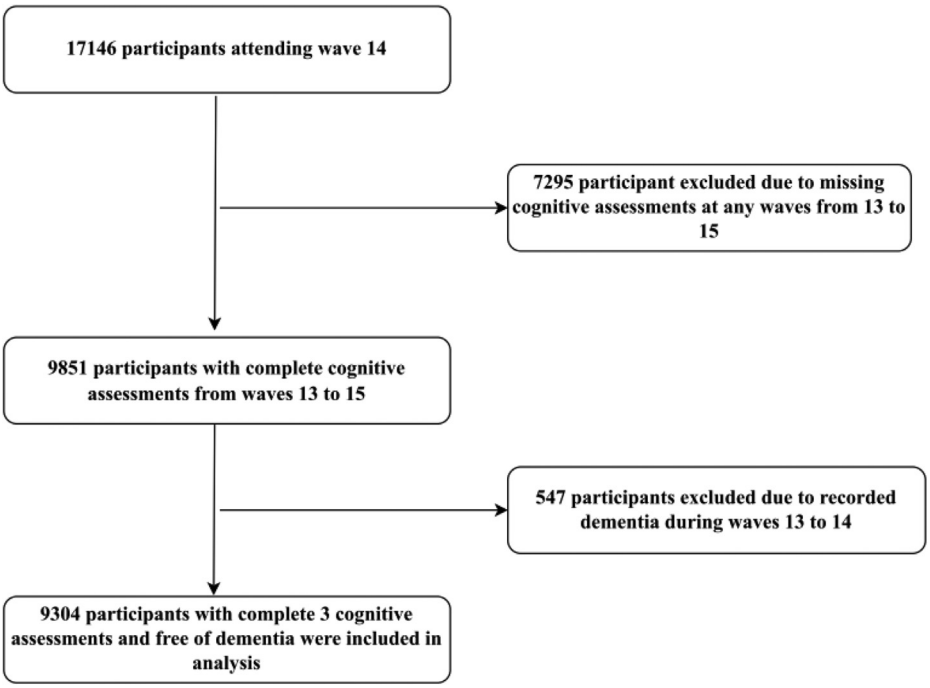
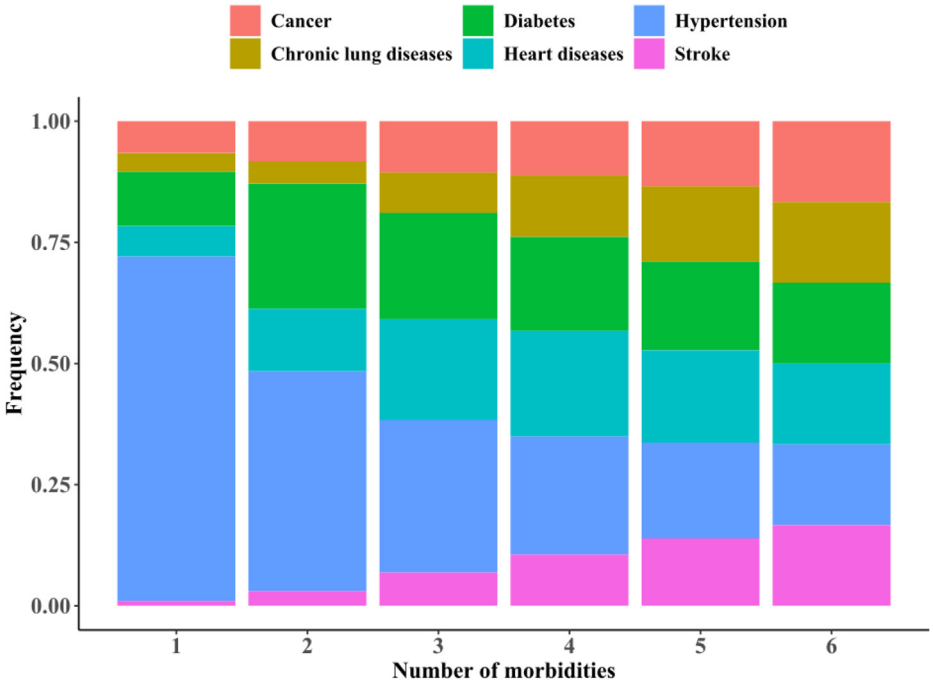
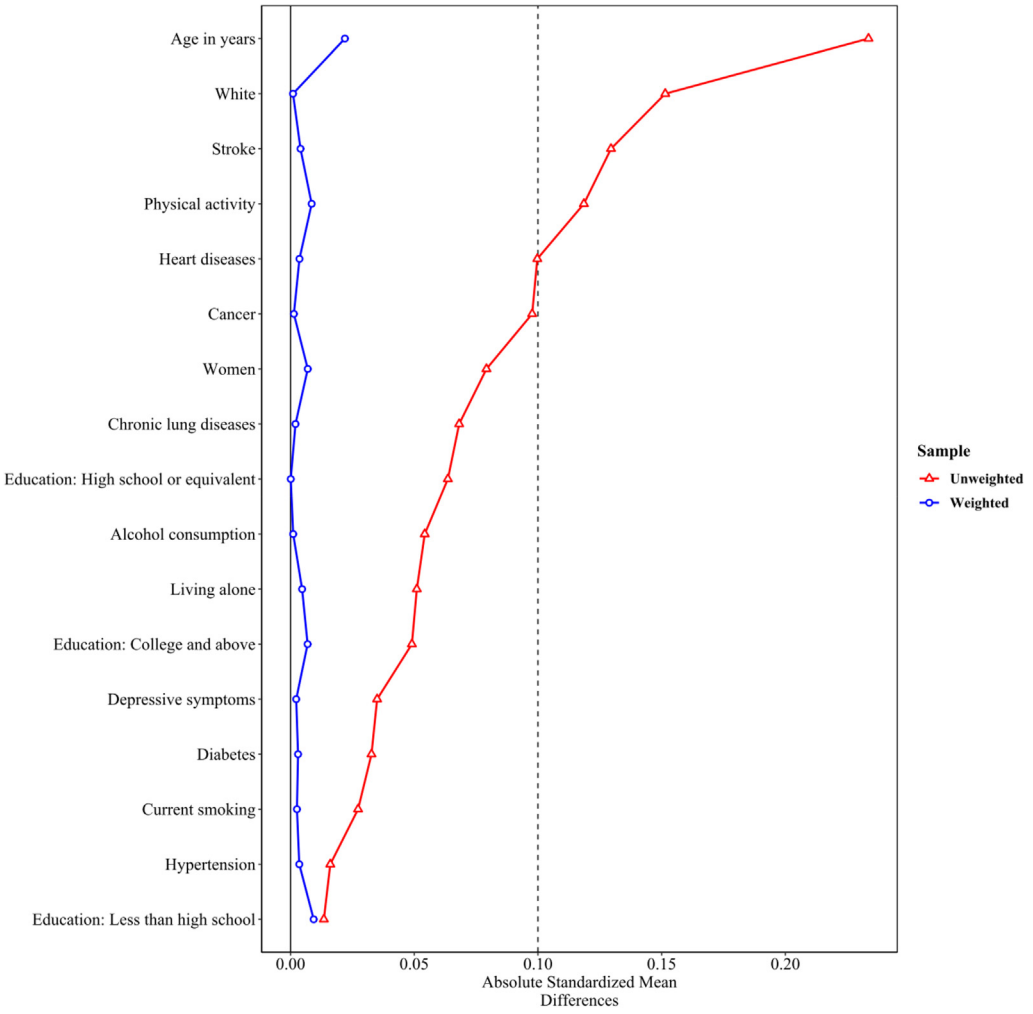


Supplementary Fig. 1. Participants selection diagram.



Supplementary Fig. 2. The distribution of morbidities.



Supplementary Fig. 3. Love plot assessing differences in characteristics between included and excluded participants in HRS, based on the original unweighted and IPW samples, respectively.

Supplementary Table 1
Mean Differences in Changes of Global Cognition *z* Score During the Pandemic Period Between Multimorbidity status Groups, Adjusting for Each of the 6 Chronic Diseases Individually

Multimorbidity Status	Adjusted differences (95% CI)	*P*
Without adjusting for chronic diseases*		
No morbidity	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497
≥2 morbidities	−0.08 (−0.13, −0.03)	.003
Adjusted for hypertension		
No morbidity	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497
≥2 morbidities	−0.08 (−0.13, −0.03)	.003
Adjusted for diabetes		
No morbidity	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497
≥2 morbidities	−0.08 (−0.13, −0.03)	.003
Adjusted for stroke		
No morbidity	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497
≥2 morbidities	−0.08 (−0.13, −0.03)	.003
Adjusted for heart diseases		
No morbidity	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497
≥ 2 morbidities	−0.08 (−0.13, −0.03)	.003
Adjusted for chronic lung diseases		
No morbidity	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497
≥2 morbidities	−0.08 (−0.13, −0.03)	.003
Adjusted for cancer		
No morbidity	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497
≥2 morbidities	−0.08 (−0.13, −0.03)	.003

*Covariates adjusted including age, sex, education background, race, cohabitation status, current smoking, alcohol consumption, physical activity participation, and depressive symptoms.

Supplementary Table 2
Associations Between Multimorbidity Status and Incident Dementia During the Pandemic, Adjusting for Each of the 6 Chronic Diseases Individually

Multimorbidity Status	RR (95% CI)	*P*
Without adjusting for chronic diseases*		
No morbidity	Reference	/
1 morbidity	1.31 (0.82, 2.11)	.258
≥2 morbidities	1.66 (1.05, 2.61)	.029
Adjusted for hypertension		
No morbidity	Reference	/
1 morbidity	0.98 (0.54, 1.78)	.958
≥2 morbidities	1.17 (0.62, 2.19)	.624
Adjusted for diabetes		
No morbidity	Reference	/
1 morbidity	1.30 (0.81, 2.08)	.284
≥ 2 morbidities	1.54 (0.94, 2.51)	.087
Adjusted for stroke		
No morbidity	Reference	/
1 morbidity	1.31 (0.82, 2.11)	.260
≥2 morbidities	1.62 (1.03, 2.57)	.039
Adjusted for heart diseases		
No morbidity	Reference	/
1 morbidity	1.31 (0.82, 2.11)	.257
≥2 morbidities	1.68 (1.06, 2.66)	.028
Adjusted for chronic lung diseases		
No morbidity	Reference	/
1 morbidity	1.32 (0.82, 2.13)	.246
≥2 morbidities	1.72 (1.09, 2.73)	.021
Adjusted for cancer		
No morbidity	Reference	/
1 morbidity	1.31 (0.81, 2.10)	.268
≥2 morbidities	1.62 (1.02, 2.56)	.040

*Covariates adjusted including age, sex, education background, race, cohabitation status, current smoking, alcohol consumption, physical activity participation, depressive symptoms, and baseline cognition summary score.

Supplementary Table 3
Associations of Multimorbidity Status with Incident Dementia Risk During the Pandemic, Stratified by Sex

Multimorbidity Status	Men (N = 3649)		Women (N = 5655)		*P* for Interaction
	RR (95% CI)*	*P*	RR (95% CI)*	*P*	
No morbidity	Reference	/	Reference	/	/
1 morbidity	0.98 (0.48, 2.02)	.964	1.62 (0.85, 3.06)	.140	.312
≥2 morbidities	1.00 (0.51, 1.93)	.991	2.34 (1.25, 4.39)	.008	.065

*RR was estimated using modified Poisson regression models. Adjusted covariates included age, sex, education background, ethnicity, cohabitation status, current smoking, alcohol consumption, physical activity participation, depressive symptoms, and baseline cognition score.

Supplementary Table 4
Associations of Multimorbidity Status with Incident Dementia Risk During the Pandemic, Stratified by Age

Multimorbidity Status	Age <65 y (n = 4762)		Age ≥65 y (n = 4542)		*P* for Interaction
	RR (95% CI)*	*P*	RR (95% CI)*	*P*	
No morbidity	Reference	/	Reference	/	/
1 morbidity	2.09 (0.97, 4.51)	.061	0.89 (0.49, 1.59)	.689	.083
≥2 morbidities	2.73 (1.29, 5.80)	.009	1.13 (0.65, 1.94)	.668	.062

*RR was estimated using modified Poisson regression models. Adjusted covariates included age, sex, education background, ethnicity, cohabitation status, current smoking, alcohol consumption, physical activity participation, depressive symptoms, and baseline cognition score.

Supplementary Table 5
Associations of Multimorbidity Status with Incident Dementia Risk During the Pandemic, Stratified by Whether Suffering Death From COVID-19 of Familiar People

Multimorbidity Status	Without Suffering (n = 7503)		Suffering (n = 1801)		*P* for Interaction
	RR (95% CI)*	*P*	RR (95% CI)*	*P*	
No morbidity	Reference	/	Reference	/	/
1 morbidity	1.23 (0.74, 2.05)	.430	1.80 (0.50, 6.44)	.369	.589
≥2 morbidities	1.54 (0.94, 2.52)	.084	2.32 (0.72, 7.50)	.160	.529

*RR was estimated using modified Poisson regression models. Adjusted covariates included age, sex, education background, ethnicity, cohabitation status, current smoking, alcohol consumption, physical activity participation, depressive symptoms, and baseline cognition score.

Supplementary Table 6
Associations of Multimorbidity Status with Incident Dementia Risk During the Pandemic, Stratified by Whether Suffering COVID-19 Infection of Familiar People

Multimorbidity Status	Without Suffering (n = 6030)		Suffering (n = 3274)		*P* for Interaction
	RR (95% CI)*	*P*	RR (95% CI)*	*P*	
No morbidity	Reference	/	Reference	/	/
1 morbidity	1.21 (0.71, 2.06)	.488	1.64 (0.60, 4.52)	.338	.600
≥2 morbidities	1.65 (0.99, 2.75)	.057	1.60 (0.60, 4.25)	.347	.960

*RR was estimated using modified Poisson regression models. Adjusted covariates included age, sex, education background, ethnicity, cohabitation status, current smoking, alcohol consumption, physical activity participation, depressive symptoms, and baseline cognition score.

Supplementary Table 7
Associations of Multimorbidity Status with Incident Dementia Risk During the Pandemic, Stratified by Whether Experiencing Delayed Care During the COVID-19 Pandemic

Multimorbidity Status	Without Experiencing (n = 7258)		Experiencing (n = 2046)		*P* for Interaction
	RR (95% CI)*	*P*	RR (95% CI)*	*P*	
No morbidity	Reference	/	Reference	/	/
1 morbidity	1.19 (0.71, 1.98)	.506	2.17 (0.61, 7.69)	.228	.385
≥2 morbidities	1.57 (0.97, 2.55)	.065	2.29 (0.62, 8.39)	.213	.598

*RR was estimated using modified Poisson regression models. Adjusted covariates included age, sex, education background, ethnicity, cohabitation status, current smoking, alcohol consumption, physical activity participation, depressive symptoms, and baseline cognition score.

Supplementary Table 8
Baseline Characteristics Comparison Between Participants Included and Excluded From Analysis in HRS

Characteristics*	Excluded N = 7842	Included N = 9304	*P*†
Age (y)	68.4 ± 11.9	65.8 ± 10.8	<.001
Men (%)	3381 (43.1%)	3649 (39.2%)	<.001
White (%)	5470 (69.8%)	5825 (62.6%)	.001
Living alone (%)	3163 (40.3%)	3521 (37.8%)	<.001
Education background (%)			
Less than high school	1329 (16.9%)	1530 (16.4%)	<.001
High school or equivalent	2356 (30.0%)	3070 (33.0%)	
College and above	4157 (53.0%)	4704 (50.6%)	
Current smoking (%)	989 (12.6%)	1259 (13.5%)	.079
Drinking ≥3 d per wk (%)	1406 (17.9%)	1479 (15.9%)	<.001
Physical Exercise (%)	5097 (65.0%)	6562 (70.5%)	<.001
Depressive symptoms (%)	1190 (15.2%)	1297 (13.9%)	.024
Morbidities (%)			
No morbidity	1474 (18.8%)	1818 (19.5%)	<.001
1 morbidity	2396 (30.6%)	3111 (33.4%)	
≥2 morbidities	3972 (50.7%)	4375 (47.0%)	
Hypertension (%)	5342 (68.1%)	6268 (67.4%)	.302
Diabetes (%)	2362 (30.1%)	2943 (31.6%)	.034
Stroke (%)	887 (11.3%)	701 (7.5%)	<.001
Heart diseases (%)	2124 (27.1%)	2119 (22.8%)	<.001
Chronic lung diseases (%)	989 (12.6%)	971 (10.4%)	<.001
Cancer (%)	1367 (17.4%)	1292 (13.9%)	<.001
Cognition score	14.2 ± 5.3	15.9 ± 3.9	<.001

*Data represented characteristics as mean ± SD or n (%).
†*P* value reported for differences between groups using *t* test or χ^2 test.

Supplementary Table 9
Mean Differences in Changes of Global and Subdomain Cognition *z* Scores Between Multimorbidity Status Groups Based on the IPW Sample, by Study Periods

Multimorbidity Status	Global z Score		Memory z Score		Executive Function z core	
	β (95% CI)*	*P*	β (95% CI)	*P*	β (95% CI)	*P*
Control period						
No morbidity	Reference	/	Reference	/	Reference	/
1 morbidity	−0.02 (−0.07, 0.03)	.493	−0.03 (−0.10, 0.03)	.275	0.01 (−0.05, 0.06)	.815
≥2 morbidities	−0.04 (−0.09, 0.01)	.143	−0.04 (−0.10, 0.02)	.184	−0.02 (−0.07, 0.03)	.482
Pandemic period						
No morbidity	Reference	/	Reference	/	Reference	/
1 morbidity	0.02 (−0.03, 0.07)	.464	0.04 (−0.03, 0.10)	.243	−0.01 (−0.06, 0.05)	.795
≥2 morbidities	−0.08 (−0.13, −0.03)	.003	−0.06 (−0.13, −0.00)	.039	−0.06 (−0.10, −0.01)	.025

*Adjusted for age, sex, and education background, race, cohabitation status, current smoking, alcohol consumption, physical activity participation, and depressive symptoms.

Supplementary Table 10
Associations of Multimorbidity Status with Incident Dementia Risk During the Pandemic Period, Based on the IPW Sample.

Multimorbidity Status	Risk for Incident Dementia	
	RR (95% CI)	*P*
Model 1*		
No morbidity	Reference	/
1 morbidity	1.40 (0.86, 2.29)	.176
≥2 morbidities	2.14 (1.34, 3.41)	.002
Model 2†		
No morbidity	Reference	/
1 morbidity	1.27 (0.78, 2.08)	.332
≥2 morbidities	1.81 (1.13, 2.89)	.013
Model 3‡		
No morbidity	Reference	/
1 morbidity	1.26 (0.78, 2.02)	.345
≥2 morbidities	1.58 (1.00, 2.50)	.048

*Model 1: adjusted for age, sex, and education background.
†Model 2: model 1 + race, cohabitation status, current smoking, alcohol consumption, physical activity participation, and depressive symptoms.
‡Model 3: model 2 + baseline cognition summary score.

Supplementary Table 11
Mean Differences in Changes of Global Cognition *z* Score During the Pandemic Period Between Multimorbidity Status Groups, Further Adjusting for Blood Pressure, Blood Glucose, and Corresponding Treatments

Multimorbidity Status	Global z Score		Memory *z* Score		Executive Function z core	
	β (95% CI)*	*P*	β (95% CI)	*P*	β (95% CI)	*P*
Before adjusting*						
No morbidity	Reference	/	Reference	/	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497	0.04 (−0.03, 0.10)	.263	−0.01 (−0.06, 0.04)	.776
≥2 morbidities	−0.08 (−0.13, −0.03)	.003	−0.06 (−0.12, −0.01)	.042	−0.06 (−0.11, −0.01)	.023
After adjusting†						
No morbidity	Reference	/	Reference	/	Reference	/
1 morbidity	0.02 (−0.04, 0.07)	.497	0.04 (−0.03, 0.10)	.263	−0.01 (−0.06, 0.04)	.776
≥2 morbidities	−0.08 (−0.13, −0.03)	.003	−0.06 (−0.12, −0.00)	.042	−0.06 (−0.11, −0.01)	.023

*Adjusted for age, sex, and education background, race, cohabitation status, current smoking, alcohol consumption, physical activity participation, depressive symptoms.
†Further adjusted for blood pressure status, blood glucose status, and the regular use of insulin and antihypertensive medications.

Supplementary Table 12
Associations Between Multimorbidity Status and Incident Dementia During the Pandemic, Further Adjusting for Blood Pressure, Blood Glucose, and Corresponding Treatments

Multimorbidity Status	RR (95% CI)	*P*
Before adjusting*		
No morbidity	Reference	/
1 morbidity	1.31 (0.82, 2.11)	.258
≥2 morbidities	1.66 (1.05, 2.61)	.029
After adjusting†		
No morbidity	Reference	/
1 morbidity	1.26 (0.76, 2.06)	.370
≥2 morbidities	1.52 (0.90, 2.56)	.118

*Covariates adjusted including age, sex, education background, race, cohabitation status, current smoking, alcohol consumption, physical activity participation, depressive symptoms, and baseline cognition summary score.
†Further adjusted for blood pressure status, blood glucose status, and the regular use of insulin and antihypertensive medications.

Supplementary Table 13
Associations of Multimorbidity Status According to Diabetes and Hypertension With Incident Dementia Risk During the Pandemic Period

Multimorbidity Status	Events/Total	Risk for incident Dementia	
		RR (95% CI)	*P*
Model 1*			
No morbidity	21/1818	Reference	/
1 morbidity without hypertension or diabetes	6/549	0.77 (0.31, 1.89)	.566
1 morbidity with hypertension or diabetes	64/2562	1.60 (0.98, 2.62)	.062
≥2 morbidities without the co-presence of hypertension and diabetes	701972	1.87 (1.13, 3.12)	.016
≥2 morbidities with the co-presence of hypertension and diabetes	116/2403	2.51 (1.56, 4.04)	<.001
Model 2†			
No morbidity	21/1818	Reference	/
1 morbidity without hypertension or diabetes	6/549	0.76 (0.31, 1.85)	.539
1 morbidity with hypertension or diabetes	64/2562	1.43 (0.87, 2.35)	.153
≥2 morbidities without the co-presence of hypertension and diabetes	701972	1.61 (0.97, 2.68)	.064
≥2 morbidities with the co-presence of hypertension and diabetes	116/2403	2.09 (1.30, 3.36)	.002
Model 3‡			
No morbidity	21/1818	Reference	/
1 morbidity without hypertension or diabetes	6/549	0.74 (0.31, 1.77)	.502
1 morbidity with hypertension or diabetes	64/2562	1.42 (0.88, 2.29)	.156
Confidence	701972	1.44 (0.88, 2.35)	.150
Confidence	116/2403	1.81 (1.14, 2.89)	.012

*Model 1: adjusted for age, sex, and education background.
†Model 2: model 1 + race, cohabitation status, current smoking, alcohol consumption, physical activity participation, and depressive symptoms.
‡Model 3: model 2 + baseline cognition summary score.